AUTOMATED FEEDBACK CONTROL OF HEMODIALYSIS SYSTEM

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Abstract- **We present a framework system dynamics (simulation) model that evaluates the effect of dialysis policies on session performance, quantifying, optimizing dialysis efficiency and monitoring dialysis performance online. The model focuses on analyzing and highlights factors which may alter the delivered dose and may lead to session degradation This will help increase the achievement of adequate Hemodialysis to a level consistent with or higher than National Adequacy Statistics, in order to reduce the Morbidity rate of the Hemodialysis patient. Five blood samples were drawn from 134 dialysis patient; arterial sample at the inlet of the dialyzer, venous sample at the outlet of the dialyzer, peripheral sample, pre blood urea sample and post blood urea sample. The simulation results and the statistical analysis revealed that there is no statistically significant difference between the calculated results and the measured results. This system dynamics model is considered the first system that calculates the dialysis session performance as a function of not only dialysis adequacy but also as a function of the intradialytic complications and overall equipment effectiveness.**

Keywords-**Hemodialysis, Optimum hemodialysis dose, Formal Urea kinetic modeling, Hemodialysis adequacy Kt/V, System Dynamics.**

I. INTRODUCTION

The fractional urea clearance model for hemodialysis is expressed as Kt/V, where K is dialyzer clearance (ml/min), t is treatment time (min), and V is total-body urea distribution volume [1,2,3,4]. A simpler and more common measurement of fractional urea clearance during a single dialysis treatment is the urea reduction ratio (URR) [5,6]. This ratio is expressed as a percentage and is calculated as [(pre-dialysis Blood urea nitrogen minus post-dialysis Blood urea nitrogen) / pre-dialysis Blood urea nitrogen]*100. An approximate relationship between these two means of expressing dialysis dose can be made: Kt/V of 1.2 is approximately equal to URR 60 percent. Recent reports demonstrated a direct correlation between dialysis mortality and Kt/V (or URR) [7,8,9,10]. Several studies have also suggested that the dialysis dose delivered to many hemodialysis patients in Egypt was less than that recommended by the National Cooperative Dialysis Study. As changes in Kt/V may be paralleled by corresponding changes in net protein catabolic rate, dietary protein intake may decrease if the dialysis prescription fails to achieve the desired goal and the patient becomes symptomatic [11]. Attainment of the recommended Kt/V is influenced by a number of factors, modifiable and unmodifiable, which may alter the delivered dose [12,13]. These factors include, but are not limited to: toxin removal rate, protein catabolic rate, estimation of residual kidney function, vascular access, equipment efficiency, patient factors and kinetics of fluid compartment shifts. All of this information can be useful to the physician when deciding how well the prescribed treatment is helping the dialysis patient. In order to optimize and manage the relationships between the factors that may alter the delivered dialysis dose, it is very important to understand the dynamics behind these factors and provides a control feedback to evaluate the impact of critical dialysis parameters on dialysis session performance. System dynamics is an approach that investigates the information feedback characteristics of dynamic systems and shows how structure, policies, decisions and delays interact to influence system growth and stability [14,15].

II. METHODOLOGY

A. Research Design

The research analysis started by developing the mental model (Dialysis performance causal loop diagram), explaining and understanding the complex cause and effect relationships existing between different policy elements. Arriving at that stage, the following objectives can be accomplished:

Building a System Dynamics performance assessment framework model for monitoring hemodialysis session performance online, Identifying the performance drivers in the hemodialysis session management process, Investigating and understanding the dynamic behavior that characterizes the hemodialysis session management process and formulating, analyzing and comparing various policies to determine optimum level of dialysis parameters for improved session performance. To accomplish such objective, a simulation model using stock and flow diagrams will be designed through the aid of Vensim DSS32 version 4.0a software. For the purpose of building the stock & flow diagram and to structure the transformation process of the causal loop diagram (equations, historical relationships or assumed functions/curves), the researchers used a methodology named as the "stock & flow mapping"[1]. Please refer to Appendix A for details on the mapping cards design. Depending on the availability and complexity of the data

[1] This methodology was developed specially for the purpose of this research with the professional guidance of Dr. Khaled Wahba. The idea is to create one mapping card per key leverage causal loop variable. A mapping card then would include the design for only one level of the stock & flow diagram (level of the mapped variable) identifying stocks, flows, converters, units, equations, graphs…etc

needed as well as sample size; a data collection tool was designed specifically for this purpose (model formulation phase). The simulation model will then be validated (model evaluation phase) for the analysis (policy analysis phase). Finally, the research concludes findings from the data analysis.

B. Model Description

What is the Hemodiadynamics?! Hemodiadynamics is the name of our model. It refers to "Hemodialysis dynamic system". The Hemodiadynamics is a system dynamics software used to analyze and identify the important implications for a successful implementation of a Hemodialysis session Performance. Hemodiadynamics can be considered as a new urea kinetic modeling used for monitoring and assessing dialysis efficiency online. The functions of this software can be summarized as following: 1. Calculate the dialysis Adequacy (Kt/V) and show its increase over time (on line adequacy monitoring, 2. Estimate the Post BUN and show the reduction of Blood Urea Nitrogen (BUN) over time (On line BUN reduction monitoring), 3. Calculate the urea distribution Volume and show its reduction over time (On line urea distribution monitoring), 4. Estimate the in vivo dialyzer clearance, 5. Estimate the Recirculation of the vascular access, 6. Estimate the pre BUN for the next dialysis session and 7. Calculate the overall session performance as a function of the delivered dialysis adequacy, overall equipment effectiveness and the intradialytic complications.

Figure 1 shows the overall Causal Loop Diagram (CLD) of the Hemodiadynamics. Causal loop diagram is a useful tool to map feedback loops and causal relationships among individual variables. Arrow originates from cause and leads to effect denoting the causal influence among variables and its polarity indicate the direction of effect with respect to cause. Thus causal loop diagrams are excellent for quickly capturing the hypothesis about the cause of dynamics, eliciting and capturing the mental models and communicating important feedbacks [14]. The causal loop diagram shown below is divided into two models: (1) The intradialytic model (during dialysis session) which analyzing the dynamic behavior of various factors that characterizes and controlling the hemodialysis session management process and (2) The interdialytic model (between dialysis sessions) which identifying the effect of increasing dialysis adequacy on nutritional status of the patient which in turn reduces the morbidity rate and the intradialytic complications. The various feedback loops manifested in the causal loop diagram are described in detail in appendix A. The important loops are highlighted by a loop identifier which shows whether the loop is a positive (reinforcing) or negative (balancing) feedback. The loop identifier R represents a reinforcing loop (positive feedback) and the loop identifier B represents a balancing loop (negative feedback). Note that the loop identifier circulates in the same direction as the loop to which it corresponds.

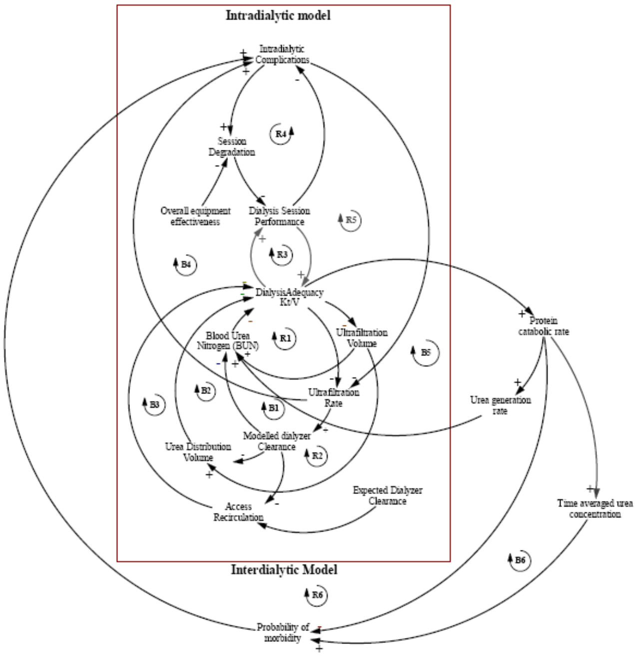

Fig.1. The Overall Causal Loop Diagram Of Hemodiadynamics

C. Formulating a Simulation Model (Stock & Flow Diagram)

This next step in modeling involves setting up a formal model complete with equations, parameters and initial conditions that represent the system. Sometimes the dynamic hypotheses can be tested directly through data collection or experiments in the real system. Causal loops are useful to represent the interdependencies and feedback processes and to capture mental models at the beginning of the modeling process. However, one of the most important limitations of the causal diagrams is their inability to capture stock and flow structure of systems. Stocks and flows, along with feedback, are the two central concepts of dynamic systems theory. Stocks are accumulations that occur as a result of a difference in input and output flow rates to a process/component in a system. Stocks give the systems inertia and memory, based on which decisions and actions are taken. Stocks also create delays in a system and generate disequilibria [14]. Figure 2 represents the general structure of a stock and flow. All stock and flow structures are composed of stocks (represented by rectangles), inflows (represented by arrows pointing into the stock), outflows (represented by arrows pointing out from the stock), valves, sources and sinks for flows (represented by clouds).

Fig. 2 General Structure of a Stock and Flow

Mathematically, equations for the stock element can be formulated as follows:

$$\text{Stock}(t) = \text{Stock}(t_0) + \int [\text{Inflow}(t) - \text{Outflow}(t)]\,dt \qquad (1)$$

Hence, the value of stock at time t is the sum of the value of stock at time t_0 and the integral of difference between inflow and outflow rates from t_0 to t. In other words, we can also state that the rate of change in stock at any point in time is equal to the difference between inflow and outflow at that point. The stock and flow structure has a one-to-one correspondence to the causal loop structure presented earlier. The outcome of the mapping cards is a full design of the stock & flow graphical notation ready to be coded into the computer using a software package such as Vensim DSS [16]. Moreover, the mapping cards also revealed the data needed to be collected and input to the simulation model for validation before final simulation and policy analysis. The overall stock and flow diagram is shown in figure 3. The stock and flow diagram has been divided into five subsystems, 1) The modeled dialysis adequacy (Kt/V) subsystem, 2) The modeled post bun subsystem, 3) The urea distribution volume subsystem, 4) The ultrafiltration volume subsystem, and 5) The overall dialysis session performance subsystem. For each subsystem the assumed parameters, initial values, variable were ranged to be entered to the system for the sake of building the stock & flow diagram. After that the equations and graphs that describe the relationships between the various variables were entered to the system using the vensim DSS software and were elicited from the experts in the field of nephrology [17]. They were asked for their inputs on the units for measurement of different variables, the functional form of the various equations between variables, parameters of these equations (elicited through graphical portrayal of key relationships), and the initial values of all stock variables.

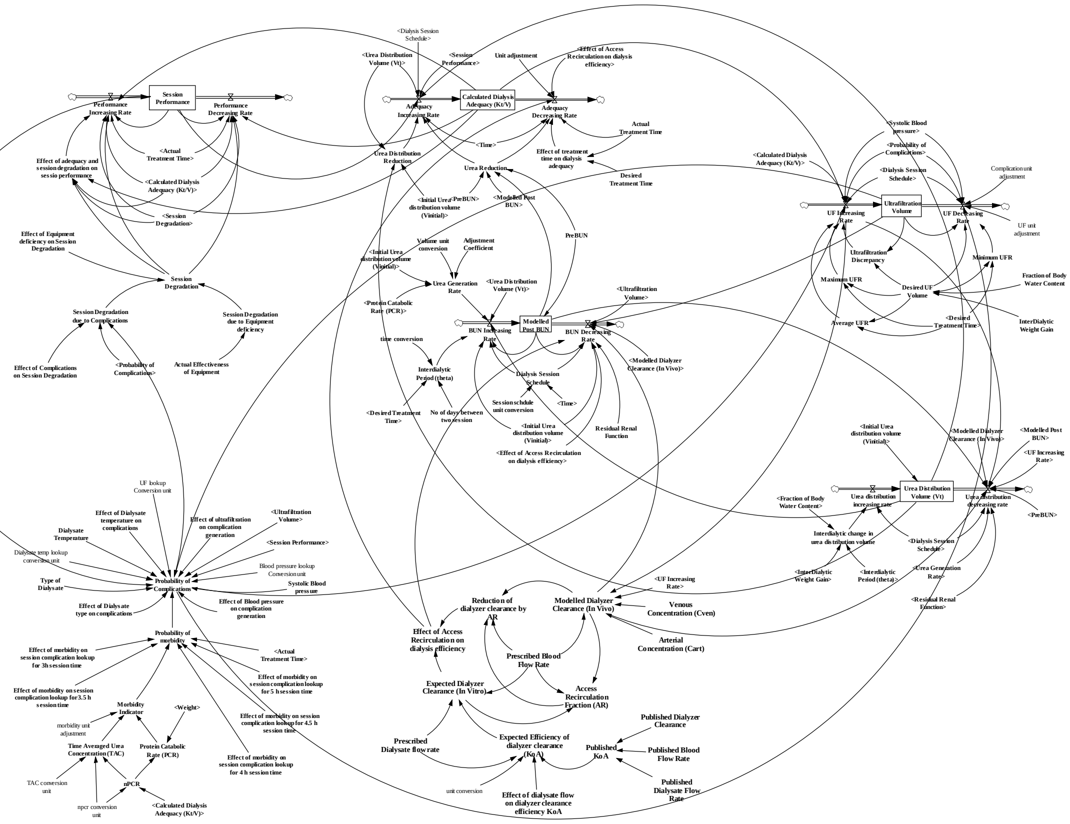

Fig. 3 The Overall Stock And Flow Diagram Of Hemodiaynamics

III. RESULTS

1. Statistical analysis

Five blood samples were drawn from 134 dialysis patient; arterial sample at the inlet of the dialyzer, venous sample at the outlet of the dialyzer, peripheral sample, pre blood urea sample and post blood urea sample. The post blood urea sample was drawn at different dialysis times-180 min (3 hours), 189 min (3.15 hours), 225 min (3.75 hours) and 240 min (4 hours)-to validate the results of our dynamical model with the measured results. Statistical analysis was performed using SPSS 12.0 and NCSS 2004. The following tests were done to validate our results:

A. Paired sample T-tests were used to compare the means and B. F-tests were used to compare the variation between: Delivered (measured) Kt/V with the calculated Kt/V by

Hemodiadynamics, measured post BUN with the estimated post BUN by our model and measured recirculation fraction with the estimated recirculation by the model. Hence, the statistical analysis revealed that there is no statistically significant difference between the calculated Kt/V by our system dynamics model and the measured Kt/V (P-value = 0.552), no difference existed between the measured post blood urea and the estimated one by our system (P-value = 0.091) and there is no statistically significant difference between the calculated recirculation fraction and the measured one (P-value = 0.156). The model was subjected to several validity tests, such as checking the model's mathematical equations in relation to the causal loop signs; checking the units' consistency between the model's variables, and finally running the model at extreme values in order to identify any unrealistic behavior [18,19,20].

2. Sensitivity analysis

Data input to the system and assumptions are validated using sensitivity analysis in order to ensure that the model behaves normally when such values are varied over a reasonable range. Eight tests were performed as follows where the model yielded an expected behavior in all tests. (1) Effect of increasing dialyzer clearance on session performance, (2) Effect of increasing blood flow rate on session performance, (3) Effect of increasing dialysate flow rate on session performance, (4) Effect of increasing ultrafiltration rate on session performance, (5) Effect of residual renal function on urea reduction, (6) Effect of intradialytic complications on session performance, (7) Effect of session degradation due to complications and equipment effectiveness on session performance, (8) Effect of Access Recirculation on dialysis adequacy. For example the sensitivity analysis of tests from 1-3 are shown in figures 4, 5 and 6. The first three effects were simulated with four sets of key parameter combinations, namely, (1) High efficiency high flux dialysis (2) Conventional efficiency dialysis (High efficiency low flux dialysis), (3) Low efficiency dialysis with high blood flow rate and (4) Low efficiency low flux dialysis. The parameter sets were:

Parameter Set 1 (High Efficiency High flux Dialysis): High blood flow rate (Q_b = 330 ml/min), High dialysate flow rate (Q_d = 800 ml/min) and High dialyzer clearance (K_d = 245 ml/min)

Parameter Set 2 (Conventional Efficiency Dialysis or High efficiency low flux dialysis): Conventional blood flow rate (Q_b = 300 ml/min), High dialysate flow rate (Q_d = 800 ml/min), High dialyzer clearance (K_d = 229 ml/min).

Parameter Set 3 (Low Efficiency Dialysis with high blood flow rate): Conventional blood flow rate (Q_b = 300 ml/min) , Low dialysate flow rate (Q_d = 500 ml/min), Low dialyzer clearance (K_d = 202 ml/min).

Parameter Set 4 (Low Efficiency low flux dialysis): Low blood flow rate (Q_b = 250 ml/min), Low dialysate flow rate (Q_d = 500 ml/min), Low dialyzer clearance (K_d = 182 ml/min).

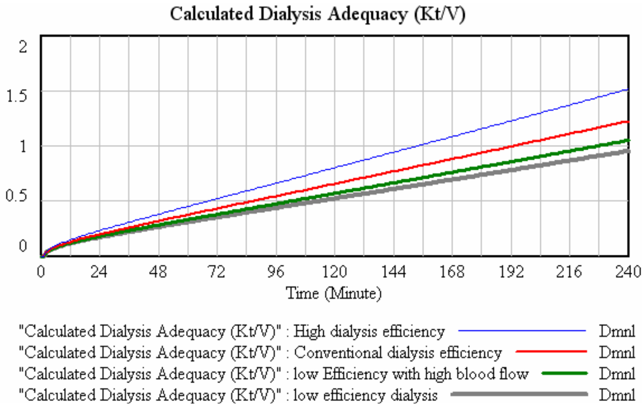

Fig.4. Dialysis Adequacy (Kt/V) at Four Sets of Parameter Inputs

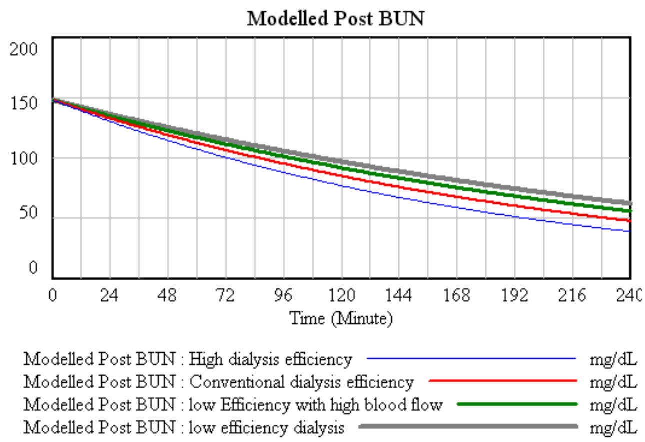

Fig.5. Modelled Post-BUN at Four Sets of Parameter Inputs

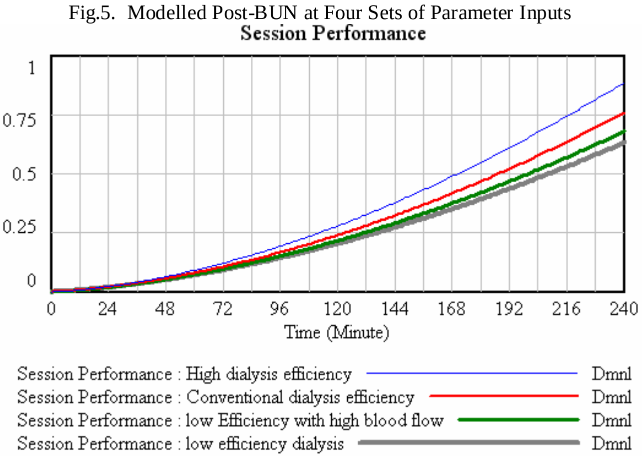

Fig.6. Dialysis Session Performance at Four Sets of Parameter Inputs

IV. Discussion And Conclusion

Over the last decade, the concept of dialysis adequacy has evolved to become a component of the optimal dialysis that includes quantitative and qualitative aspects. Current method used to assess dialysis efficacy in end stage renal disease (ESRD) patients relies on a targeting approach using several vital indicators. Dialysis quality is a complex and evolutionary concept that has to be viewed in a quality assurance process to improve outcomes of ESRD patients. To simplify this assessment it is very important to understand the dynamic complexity of implementing adequate hemodialysis dose and their impact of dialysis session performance. Identifying the factors that contribute to this complexity and analyzing the interactions among them can possibly help us make better decisions and help staff achieve the desired dialysis performance, assist in development of a support system for staff to improve their reporting, assessment, and decision making processes and assist staff to make the correct responses to poor processes of care that impede adequate dialysis. The outcome of this research can directly be used by decision makers to formulate various policies in the light of assumptions and constraints of the model. Many researchers have tried to address the issue of dialysis performance by Formal urea kinetic modeling (UKM) that provides a quantitative method for developing a treatment prescription for a specific patient. But no work has been done in the past to analyze this issue from a systems perspective. Most of the mathematical models fail to capture the feedback structures that are undoubtedly inherent in any kind of system and have considerable impact on the performance of the hemodialysis system. Therefore, this software is considered the first system that can be used for on line dialysis monitoring from a systems perspective.

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Appendix A
Key Leverage Causal Loops

No.	Loop Name	Loop Route	Loop Description	Direction
1	The Effect of BUN reduction on dialysis adequacy	Calculated Dialysis Adequacy (Kt/V) - Ultrafiltration volume-Blood Urea Nitrogen (BUN).	As dialysis adequacy increases, the Ultrafiltration volume decreases and hence the blood urea nitrogen decreases which in turn increases the dialysis adequacy	R
2	The Effect Of urea distribution reduction on Kt/V	Calculated Dialysis Adequacy (Kt/V) – Ultrafiltration volume–Urea distribution volume (Vt).	As dialysis adequacy increases, the Ultrafiltration volume decreases and hence the urea distribution volume decreases which in turn increases the dialysis adequacy.	R
3	The Effect of Ultrafiltration on urea clearance.	Calculated Dialysis Adequacy (Kt/V) – Ultrafiltration rate– modeled dialyzer clearance–blood urea nitrogen (BUN).	Decrease in dialysis adequacy can force us to increase it by increasing the Ultrafiltration rate to a value not affects the patient blood pressure. Thus increase in Ultrafiltration rate will increase the in vivo dialyzer clearance and hence the blood urea nitrogen decreases which ultimately increases the dialysis adequacy.	B
4	Effect of Ultrafiltration on urea distribution volume	Calculated Dialysis Adequacy (Kt/V) – Ultrafiltration rate–modeled dialyzer clearance–Urea distribution volume (Vt).	Ultrafiltration (UF) is assumed to enhance urea removal during hemodialysis (HD) because of convective transport and because of contraction of urea distribution volume. Decrease in dialysis adequacy can also force us to increase it by increasing the Ultrafiltration rate to a value not affects the patient blood pressure. Thus increase in Ultrafiltration rate will increase the in vivo dialyzer clearance and hence the urea distribution volume decreases which ultimately increases the dialysis adequacy.	B
5	Effect of access recirculation on dialysis adequacy	Calculated Dialysis Adequacy (Kt/V) – Ultrafiltration rate–modeled dialyzer clearance–access recirculation.	When the Ultrafiltration rate increases, the modeled dialyzer clearance will increase. This increase in modeled dialyzer clearance will decrease the discrepancy between it and the expected clearance. Hence the recirculation fraction decreases which ultimately increases the dialysis adequacy.	B
6	Adequacy is the cause of performance	Calculated Dialysis Adequacy (Kt/V) – Dialysis session performance	The dose of dialysis is considered to play the major role, and has been shown to be highly associated with increased morbidity and mortality in end-stage renal disease patient population. As dialysis adequacy increases, it increases the session performance which in turn increases the delivered dialysis dose.	R
7	Complications reduces session performance	Probability of complications – session degradation – dialysis session performance	Increases in the intradialytic complications will increase the session degradation which in turn decreases the session performance. Decrease in session performance increases the probability of complications.	R

8	Effect of Ultrafiltration on complication	Ultrafiltration Rate – probability of complications	Hemodialysis-induced hypotension is still a severe complication in spite of all the progress in hemodialysis treatment. Because of its multifactorial causes, hemodialysis-induced hypotension cannot be reliably prevented by conventional ultrafiltration and sodium profiling in open-loop systems, as they are unable to adapt themselves to actual decreases in blood pressure. Increases the intradialytic complications force us to decrease the Ultrafiltration rate to decrease it. This loop is considered the ultrafiltration controller to reduce the hypotension episodes for dialysis patients. Hence, the simultaneous computer control of ultrafiltration has proven the most effective means for automatic blood pressure stabilization during hemodialysis treatment.	B
9	Effect of complication on urea removal	probability of complications – Ultrafiltration Rate – blood urea nitrogen- Calculated Dialysis Adequacy (Kt/V) – Dialysis session performance	As the complications increases, the Ultrafiltration decreases which causes the reduction of urea not to reach to a level that increases the dialysis dose and hence the dialysis session performance will decrease.	R
10	Dialysis adequacy improves nutritional status if the patient.	Calculated Dialysis Adequacy (Kt/V) – protein catabolic rate– urea generation rate- blood urea nitrogen	The balance between urea removal and urea generation will determine the urea pool and the urea concentration for a given volume of distribution. It is postulated that this urea concentration in some way causes «biofeedback » determining the protein intake of a given patient which, of course, will influence the PCR and hence, the urea generation. Therefore, increase the dialysis dose will increase the nutritional status of patient. Increase in the PCR increases the urea generation rate which increases the urea removal during session and hence increasing the dialysis adequacy.	B
11	Effect of nutritional status on morbidity rate	session degradation–dialysis session performance- Calculated Dialysis Adequacy (Kt/V) – protein catabolic rate– Probability of morbidity (session failure)–Probability of complications	Increase in nutritional status will decrease the probability of patient morbidity which will reduce the probability of intradialytic complications. Hence the session degradation will decrease which increases the session performance and in turn the dialysis adequacy.	R
12	Effect of time averaged urea concentration (TAC) on patient morbidity	session degradation- dialysis session performance- Calculated Dialysis Adequacy (Kt/V) – protein catabolic rate– time averaged urea concentration (TAC) Probability of morbidity (session failure)- Probability of complications	As the PCR increase the TAC will also increase which reduces the probability of patient morbidity. Hence the intradialytic complications will decrease which in turn increases the dialysis performance.	B